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Case Report

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Photodermatit developed with pirfenidone treatment in patient diagnosed with IPF

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ABSTRACT

Idiopathic pulmonary fibrosis (IPF) is the most common of the major idiopathic interstitial pneumonia (IIP) of unknown etiology, often presenting in advanced age, limited to the lungs, characterized by histopathologically and/or radiologically usual interstitial pneumonia (UIP) pattern, and progressing with chronic, progressive fibrosis. is the most common form. Since IPF is a disease with irreversible fibrosis, there is no curative treatment except lung transplantation. The aim of the treatments given is to stop the progression of the disease, to prevent exacerbations and to prolong the survival time (1). The greatest improvement in the treatment of IPF in recent years has been the use of antifibrotic drugs (Pirfenidone and nintedanib) that prevent fibrosis developing in the lung parenchyma (2). In this case, we aimed to present the side effect of photodermatitis in a patient who applied to our outpatient clinic with complaints of shortness of breath and cough for many years and was diagnosed with IPF and started on pirfenidone treatment.

Keywords: Pirfenidone, photosensitivity reaction, idiopathic pulmonary fibrosis

INTRODUCTION

Idiopathic pulmonary fibrosis (IPF) is the most common of the major idiopathic interstitial pneumonia (IIP) of unknown etiology, often presenting in advanced age, limited to the lungs, characterized by histopathologically and/or radiologically usual interstitial pneumonia (UIP) pattern, and progressing with chronic, progressive fibrosis. is the most common form. Since IPF is a disease with irreversible fibrosis, there is no curative treatment except lung transplantation. The aim of the treatments given is to stop the progression of the disease, to prevent exacerbations and to prolong the survival time.[1] The greatest improvement in the treatment of IPF in recent years has been the use of antifibrotic drugs (Pirfenidone and nintedanib) that prevent fibrosis developing in the lung parenchyma.[2] In this case, we aimed to present the side effect of photodermatitis in a patient who applied to our outpatient clinic with complaints of shortness of breath and cough for many years and was diagnosed with IPF and started on pirfenidone treatment.

CASE

A 56-year-old male patient was admitted to our outpatient clinic with the complaints of cough and shortness of breath increasing with exertion for many years. There was no known history of additional disease. He had a 20 pack/year history of smoking up to 10 years ago. He had no history of alcohol use. There was no previous tuberculosis or contact history. He worked as a construction worker and was also engaged in agriculture and animal husbandry. On examination, there were bibasilar inspiratory rales. High-resolution lung tomography showed a peripheral honeycomb appearance, more prominent in the lower lobes, in both lung parenchyma, and tubular bronchiectasis and peribronchial thickness increases in these areas (**Figure 1**). Findings were consistent with interstitial lung disease. The presence of connective tissue disease was investigated in the patient. ANA profile, complements, CCP and anti DS-DNA were found to be normal. Active rheumatological disease was not considered in the rheumatology consultation. Dry eye was detected with Shirmer test and treatment was started for eye diseases. Afterwards, the patient underwent diffusion test (DLCO). DLCO/VA: 66% was measured (**Figure 2**). FVC was measured as 58.3% in pulmonary function test (PFT) (**Figure 3**). The patient was diagnosed with IPF and we started Pirfenidone treatment. During the 8-month treatment period with pirfenidone, the patient, who was followed up stably and did not develop any acute exacerbation, developed erythematous, edematous and locally dry, itchy skin lesions on his hands as a result of exposure to sunlight (**Figures 4 and 5**). We thought that a rare side effect of pirfenidone could be a photosensitivity reaction. We terminated the pirfenidone treatment and we saw a regression in the patient›s lesions in 20 days (**Figure 6 and 7**).

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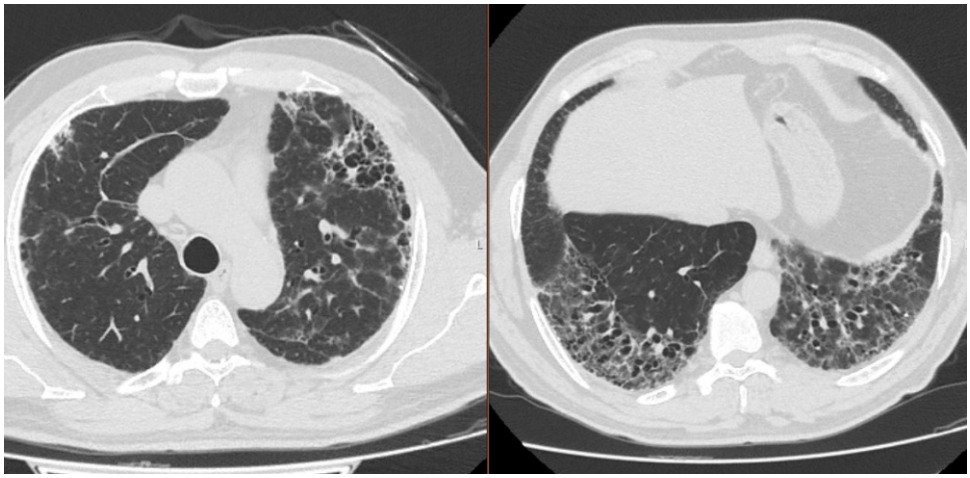

Figure 1. Patient's Chest CT at the time of diagnosis.

		Pred	Best	%(Best/Pred)
DLCO_SB	mmol/(min*kPa)	8.65	7.86	91
KCO_SB	mmol/(min*kPa*L)	1.40	1.97	141
VA_SB	L	6.03	4.00	66
Hb	g(Hb)/dL		15.00	
DLCOcSB	mmol/(min*kPa)	8.65	7.77	90
KCOc_SB	mmol/(min*kPa*L)	1.40	1.94	139
BHT	sec		11.83	
VIN_SB	L	3.88	2.35	61
TLC_SB	L	6.18	4.18	68
FRC_SB	L	3.31	3.48	105
ERV_SB	L	1.11	1.65	149
RV_SB	L	2.20	1.82	83
RV%TLC_SB	%	36	44	121
VA_SB	L	6.03	4.00	66
IC_SB	L	2.77	0.70	25
Level date			16.06.22	
Level time			09:01	

Figure 2. Patient's DLCO test result at the time of therapy beginning.

	Pred	Pre(L)	Pre(%)
VC MAX	3.91	2.20	56.2
IC	2.79		
ERV	1.12		
FVC	3.77	2.20	58.3
FEV 1	3.02	2.17	71.7
FEV1%M	77.13	98.71	128.0
PEF	7.93	7.03	88.5
FEF 25	6.97	7.03	100.8
FEF 50	4.21	6.01	142.9
FEF 75	1.54	2.90	188.7
MMEF	3.51	5.06	144.1

Figure 3. Patient's PFT results at the time of therapy beginning.

Figure 4. Skin lesions occures on the right hand with treatment of pirfenidone.

Figure 5. Skin lesions occures on the lelf hand with treatment of pirfenidone.

Figure 6. Skin lesions on the right hand regressed after withdrawal of the pirfenidone.

Figure 7. Skin lesions on the left hand regressed after withdrawal of the pirfenidone.

DISCUSSION

In the development of IPF, recurrent micro-damages first affect the alveolar epithelium. In the abnormal healing process after epithelial damage, myelofibroblast, fibroblast and collagen accumulation is seen as a result of the disturbed balance between fibrotic and antifibrotic mediators. Afterwards, tissue damage, fibrosis and honeycomb cysts occur (2) Antifibrotic agents are recommended as the first treatment option in treatment.

Pirfenidone is a drug with antifibrotic and anti-inflammatory effects; however, the mechanism of action is not fully known. It is thought to act by inhibiting the TGF-β pathway, preventing proliferation of fibroblasts and differentiation into myofibroblasts.[3]

Studies show that the use of pirfenidone significantly reduces IPF-related mortality. In addition, fewer acute exacerbations and a decrease in adverse events are shown in IPF patients.[4]

The first study on pirfenidone was conducted on 54 IPF patients with severe fibrosis, and it was reported that it was well tolerated and stabilized respiratory functions.[5] In the multicenter randomized double-blind placebo-controlled Phase 2 study conducted by Azuma et al.[6], a significant improvement was demonstrated in the 6-minute walking test at the end of 6 and 9 months of treatment in the subgroup that maintained SpO2 value over 80%.

Oral administration of pirfenidone has rapid absorption, high bioavailability, and wide distribution. It is slowly absorbed when taken with food and reaches its maximum plasma concentration in 2.5-4 hours. It is mainly metabolized by CYP1A2. The starting dose of pirfenidone is 800 mg/day (4x200 mg/day) and the minimum effective dose is 1200 mg/day. In weekly follow-ups, it is aimed to increase the dose to 2400 mg/day.[7] Since smoking has a CYP1A2-inducing effect, smoking should be stopped before and during the treatment.[8]

The most common side effects of pirfenidone are; skin (28-51%; rash and photosensitivity) and gastrointestinal system (5-36%; dyspepsia, anorexia, nausea, vomiting, diarrhea).[3] These side effects are mild to moderate and tolerable, and have been reported to occur early in the treatment and tend to regress over time.

Skin side effects occur on sun-exposed areas of the body as rash and photosensitivity, and this feature distinguishes it from allergic reactions. In the CAPACITY study conducted by Noble et al.[8], photosensitivity resulted in discontinuation of treatment in 3 patients and rash in 5 patients.[9] Drug-induced photosensitivity reactions depend on the drug's ability to absorb UV rays, both UVA and UVB. These side effects are proportional to UV exposure and drug dose and are temporary. Sun exposure should be avoided until 1-2 hours after taking the drug. The patient should be advised to avoid direct sunlight and fluorescent lamps, use high factor sunscreen, wear sunscreen, and stay away from photosensitizing agents.

CONCLUSION

Patient education and follow-up facilitate coping with side effects and increase the patient's treatment compliance and continuity. For this reason, the patient should be informed in detail and clearly at every stage from the diagnosis process to the treatment and follow-up of the disease.

ETHICAL DECLARATIONS

Informed Consent: All patients signed and free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution,

and analysis of the paper, and that they have approved the final version.

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